Organotypic Reconstructs of Barrett’s Esophagus

Rachelle Kosoff¹, Kirill Pavlov¹,², Kristin Gardiner¹, Lauren Merlo¹, Anil Rustgi³, Carlo Maley¹

¹The Wistar Institute, Philadelphia, Pennsylvania, USA
²University Medical Center Groningen, University of Groningen, Groningen, The Netherlands. ³Department of Medicine, University of Pennsylvania School of Medicine, Philadelphia, Pennsylvania, USA.

Background: Research in Barrett’s oesophagus (BE) is limited by a lack of good experimental models. Recently, retinoic acid (RA) was shown to induce columnar differentiation in squamous epithelium.

Methods: We have developed an organotypic in vitro reconstruct by seeding BE cells on top of collagen-embedded fibroblasts. Cell lines from normal squamous oesophageal epithelium (EPC2), a patient with metaplasia (CP-A), and patients with high grade dysplasia (CP-B, CP-C, CP-D) were cultured for three weeks under two conditions: without (control) or with 0.33uM RA. We used immunohistochemistry to investigate the expression of squamous (CK13 and CK14) and columnar (CK8, CK19, CK20) cytokeratins, MUC6, CDX2, and Alcian Blue.

Results: The squamous control reconstructs expressed CK13 and CK14. The CP-A control expresssed a mixture of squamous (CK13, CK14) and columnar (CK8, CK19) cytokeratins. The CP-B, CP-C and CP-D controls expressed CK8, CK19 and CK20. RA induced loss of CK13 and CK14 expression in the CP-A and EPC2 reconstructs, but had little influence in the CP-B, CP-C and CP-D reconstructs. We found no expression of CDX2 or MUC6 under either condition. Goblet cells were present in the CP-A reconstructs.

Conclusions: Organotypic reconstructs may be used as a model of BE. CP-A cells have a transitional phenotype between squamous and Barrett’s differentiation.